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PRINCIPAL INVESTIGATOR: Roderick J. Little, Ph.D.

CONTRACTING ORGANIZATION: University of Michigan
Ann Arbor, Michigan 48109-1274

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FOREWORD

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INTRODUCTION

The purpose of this training program in biostatistics for breast cancer research is to provide biostatisticians with the requisite scientific knowledge to understand current issues in breast cancer research, and training in statistical and epidemiological techniques and research methodology related to breast cancer. The training leads to the doctorate of philosophy in biostatistics. The methods of training include formal course work in biostatistics, epidemiology and biology related to breast cancer, interdisciplinary seminars on current research and biostatistical topics in breast cancer research, and mentored research in collaboration with biostatistics faculty and breast cancer investigators.

LEADERSHIP

The principal investigator for years 2 and 3 of the grant, KyungMann Kim, Ph.D., left the University of Michigan as of August 31, 1997 to become Director of Biostatistics at the University of Wisconsin Comprehensive Cancer Center and Professor of Statistics. With the approval of the project monitor, Professor Roderick Little assumed the directorship of the program for its fourth and final year. Dr. Little is Professor and Chair of the Department of Biostatistics, the University of Michigan School of Public Health, and Interim Associate Director of Biostatistics for the University of Michigan Comprehensive Cancer Center.

TRAINING PERSONNEL

The University of Michigan Comprehensive Cancer Center Biostatistics Core consisted of the following statistician staff: Roderick Little, Ph.D., Interim Director of Biostatistics; Daniel Normolle, Ph.D., Senior Research Associate; Myla Strawderman, M.S., Research Associate II; and Songbai Wang, M.S.P.H., Research Associate I. In addition to the mentors from the UMCCC Breast Oncology Program and from the Biostatistics Department, all four statisticians from the UMCCC Biostatistics Core play an active role in supervising the trainees and in providing guidance and supervision for interaction with the UMCCC breast cancer investigators.

TRAINING IN BIOSTATISTICS

As specified in the proposal, a seminar series on "Statistical Methods for Cancer Research" was run under the auspices of the training grant. This seminar included research presentations by faculty and trainees. A list of presentations is attached as Appendix 1. This year a specific topic was made the focus of this seminar, namely, methods for the design of Cancer Phase II clinical trials. The trainees presented seminars describing Bayesian and frequentist approaches to the design of Phase II trials, software was obtained and applied to data sets from the Cancer Center, and results were presented at three Clinical Investigator meetings involving clinicians and biostatisticians. A paper is being prepared for submission to a cancer oncology journal, and this work is forming the basis of an evaluation of the ways Phase II trials are being conducted at the University of

Michigan Comprehensive Cancer Center. All trainees have regularly attended Cancer Center Grand Rounds, as specified in Appendix 2.

For training in statistical and epidemiological techniques and research methodology relevant to and necessary for breast cancer research, the trainees are advised and required to take:

- (1) theoretical courses in statistics and probability from the Departments of Statistics and Biostatistics,
- (2) relevant methods and applied courses in biostatistics from the Department of Biostatistics, and
- (3) courses in cognate areas proposed in the original grant applications from the Departments of Epidemiology, Environmental and Industrial Health, and other Departments in the Schools of Public Health and Medicine.

The trainees have been and are involved in mentored collaborative research in breast cancer with the breast cancer researchers from the University of Michigan Comprehensive Cancer Center (UMCCC) and with the faculty from the Department of Biostatistics.

DESCRIPTION AND EVALUATION OF CURRENT TRAINEES (TASK 9)

During the 1997--1998 academic year, five doctoral students, Mr. Hua-Yun Chen, Mr. Lang Li, Ms. Leslie McClure, Mr. Gong Tang and Mr. Haicheng Tang and were supported in part on this training grant. Some reassignment of trainees was necessitated by the fact that this was the final year of the training grant, and hence other sources of support needed to be found for continuing students. Mr. Li and Mr. Gong Tang were continuing trainees from the previous year, and Mr. Chen was a previous trainee who was reassigned to the grant when his NSF funding expired. Mr. Haicheng Tang and Ms. McClure were supported for the Fall semester, but left the grant when opportunities for long-term funding became available to them. Of previous trainees, Ms. Monika Kester left the University of Michigan without pursuing her Ph.D. studies, and Mr. Rajat Mukherjee left the program to pursue his Ph.D. at the University of Wisconsin.

Hua-Yun Chen:

Mr. Chen was supported by the grant in the final year of his dissertation work. He completed his dissertation under the direction of Dr. Little in May of 1998 and has accepted a tenure-track faculty position in the Biostatistics Department at the University of Illinois at Chicago. This position will include collaboration on cancer research projects, and hence will benefit from his activities on the training grant. His paper on missing covariates in survival analysis (Chen and Little 1997), motivated by a breast cancer application, is close to be accepted for publication by the Journal of the American Statistical Association, and he has two other papers submitted for publication in major statistics journals.

Chen, H. Y. and Little, R.J.A. (1996). Proportional Hazards Regression with Missing Covariates. Under revision for *Journal of the American Statistical Association*.

Lang Li:

Mr. Li joined the training program in January of 1997. He had a 6.6 GPA in coursework in 97-98. He passed the Theory part of the Department's Part 1 Ph.D. Qualifying examination in the summer of 1997, and the Applications part in January 1998. He participated in the statistical analysis of a clinical trial on the use of oral Diethylstilbestrol for treatment of advanced prostate cancer, and collaborated with Dr. Caroline Blain in Radiology on analysis of retrospective Breast Density data. He was an active participant in the Phase II trial design study mentioned above.

Reference:

Smith DC, Redman BG, Flaherty LE, Li L, Strawderman M, Pienta KJ. A phase II trial of oral diethylstilbestrol as a second line hormonal agent in advanced prostate cancer. *Urology* (In Press)

Leslie McClure:

Leslie McClure compiled an excellent 7.67 GPA in coursework in 1997-98. She participated in meetings and seminars for the Training Grant during the semester she was a trainee, prior to taking up a longer term position as a research assistant in the Biostatistics Department.

Gong Tang:

Mr. Tang had an excellent 7.45 GPA in coursework in 1997-98, was active in the seminar project on Phase II trials, and participated in a number of research projects with Cancer Center members:

- (1). Collaboration with Dr. Susan Urba on chemotherapy and radiation therapy on head and neck cancer. A manuscript has been prepared and submitted for publication.
- (2). Collaboration with Dr. Penny Pierce on research on decision-making style on mastectomy and lumpectomy.
- (3). Analysis of breast cancer screening data, in collaboration with Dr. Kara Lubben.
- (4). Analysis on human papilloma virus data in collaboration with Dr. Elizabeth Sisk. A manuscript has been prepared and sent for publication.
- (5). Collaborative study of Laproscopic cholecystectomy injury with Dr. Pawlick.

Haicheng Tang:

Haicheng Tang had an outstanding 7.95 GPA in coursework in 1997-98, and passed both theory and application parts of the Ph.D. Part 1 qualifying examination in June, where he

received an award for best performance by a student taking the examination. While on the training grant, he participated in a research study with Dr. Jim Varani involving treatment of Human Skin-scid Mouse Transplant Data with cyclosporin. Mixed linear models were fitted using PROC GLM in SAS, and a report presenting the results of the statistical analysis was produced. Mr. Tang left the training grant in January to take a more permanent RA position.

UPDATE ON PREVIOUS TRAINEES

Monika Kester (1996-97). In 1996-97 Ms. Kester had an exceptional GPA of 8.225 in her coursework, and she worked on Dr. Chenevert's project on "Rapid 4D MRI of Gad-DTPA Enhancement for Breast Lesion Characterization," funded by the Department of Defense Breast Cancer Research Program. We were disappointed when she chose not to pursue her doctoral studies at the University of Michigan at this time, and hope she will continue her studies in the future.

Rajat Mukherjee (1996-97). Mr. Mukherjee left the Ph.D. program at Michigan for personal reasons and resumed his Ph.D. studies at the University of Wisconsin.

Daowen Zhang (1994-95) received his Ph.D. in Biostatistics in 1996 and underwent post-doctoral training with Maryfran Sowers in the Department of Epidemiology at the University of Michigan. He has accepted a tenure-track faculty position in Biostatistics at the University of Pennsylvania Medical School in the Fall of 1998. This position will entail collaboration on cancer research projects.

CONCLUSIONS AND FUTURE PLANS

The current training program terminates in the summer of 1998. We had originally planned to develop a training program in biostatistics for cancer research for submission to the National Cancer Institute (Task 9). However this plan was delayed by the loss of the grant Principal investigator and Biostatistics Core Director Dr. Kim, who was recruited by the University of Wisconsin in the summer of 1997. This was a setback, but the program continued to provide high quality training and research in biostatistics applied to breast cancer problems under the leadership of Dr. Little. Two of the most outstanding graduate students produced by the Department of Biostatistics in recent years, Daowen Zhang and Huayun Chen, were supported by the Training Grant and have gone on to assume tenure-track positions that involve cancer research as part of their responsibilities. Two other very promising Trainees, Mr. Gong Tang and Mr. Lang Li, have passed the Ph.D. Part 1 Qualifying Examination and are starting their dissertation research. One of these students will continue to be supported in the Cancer Center as a Research Assistant in 1998-99.

A national search was conducted for Dr. Kim's permanent replacement as Director of the Cancer Center Biostatistics Core this year, and Professor Jeremy Taylor accepted the position in June. Professor Taylor is currently Professor in Residence at UCLA and has

extensive experience in cancer and AIDS research at UCLA. One of his priorities when assuming the position will be to further develop ties between the Biostatistics Department and the Cancer Center at Michigan, and to write an NIH training grant for Biostatistics in Cancer Research. The experience gained from the current training grant will be invaluable when that proposal is developed.

Appendix 1.**Seminar: Statistical Methods in Cancer Research**

**Department of Biostatistics
University of Michigan School of Public Health
1997-1998**

Date	Speakers	Topic
Oct 10, 97	Hua-Yun Chen	Missing covariates in survival analysis
Oct 31, 97	Susan Murray	Sequential methods in clinical trials using the Years of Life Saved test statistic
Dec 1, 97	Lang Li	Two Frequentist Methods for the Design of Phase II Trials
Dec 8, 97	Gong Tang	Thall's Method for the Design of Phase II Trials
Jan 27, 98	BCTG Group	Phase II Trials Designs (contd)
Feb 3, 98	BCTG Group	Phase II Trial Designs (contd)
Feb 25, 98	BCTG Group	Phase II Trial Designs (contd)
March 4, 98	BCTG Group	Phase II Trial Designs (contd)
March 11, 98	BCTG Group	Phase II Trial Designs (contd)
March 18, 98	BCTG Group	Phase II Trial Designs (contd)
April 8, 98	BCTG Group	Phase II Trial Designs (contd)

**University of Michigan Comprehensive Cancer Center
Grand Rounds 1997-1998**

SEPTEMBER

5	Raymond N. DuBois Associate Professor of Medicine and Cell Biology Vanderbilt University Nashville, Tennessee	“Colorectal Cancer Prevention by NSAIDS: What are the Molecular Targets”
12	David G. Mutch, M.D. Associate Professor of Obstetrics and Gynecology Washington University Hospital	“Genetics of Endometrial Cancer”
19	Andrew Olshan, Ph.D. Associate Professor School of Public Health Department of Epidemiology University of North Carolina	“Molecular Epidemiology Head and Neck Cancer”
26	Lawrence H. Einhorn, M.D. Distinguished Professor of Medicine Hematology/Oncology Division Indiana University School of Medicine	“Update in Non-Small Cell Lung Cancer”

OCTOBER

10	John DiPersio, M.D., Ph.D. Professor of Medicine, Pediatrics and Pathology Washington University School of Medicine	“Improvement in the Supportive Care of Allogeneic Transplant Recipients”
24	Richard Chappell, Ph.D. Associate Professor of Biostatistics and Statistics University of Wisconsin-Madison	“Clinical Trials in Children’s Cancer: Some History and Scientific Issues”
31	Robert L. Capizzi, M.D. Magee Professor and Chair of the Department of Medicine Jefferson Medical College Thomas Jefferson University	“Broad Spectrum Selective Cytoprotection of Normal Tissues from Damage Associated with Cytotoxic Therapy”

**University of Michigan Comprehensive Cancer Center
Grand Rounds 1997-1998 (continued)**

NOVEMBER

7 R. Alan B. Ezekowitz, MB, ChB, Dphil
Chief of Pediatric Services
Massachusetts General Hospital
Charles Wilder Professor of Pediatrics
Harvard Medical School

“Pattern Recognition Molecules in First Line Host Defense”

14 Charles Schiffer, M.D.
Division Chief of Hematology/Oncology
Professor of Medicine
Wayne State University

“Biology and Therapeutic Consideration in the Treatment of AML”

DECEMBER

12 Ian C. MacKenzie, PhD
Professor of Dentistry
University of Michigan

“Retroviral Transduction to Investigate Epithelial Cell Growth”

19 Gary Nabel, MD, PhD
Henry Sewall Professor of Medicine
Professor of Internal Medicine and
Biological Chemistry
University of Michigan
Investigator, Howard Hughes Medical Institute

“Gene Therapy of Cancer”

1998

JANUARY

9 Robert Eisenman, Ph.D.
Member, Division of Basic Sciences
Fred Hutchison Cancer Research Center
Seattle, Washington

“Regulation of Cell Proliferation and Differentiation through a Network of Interacting Transcription Factors”

FEBRUARY

13 Gabriel Nunez, M.D.
Associate Professor of Pathology
University of Michigan

“Regulation of Programmed Cell Death”

20 Steven Gallinger, M.D., MS.c., F.R.C.S.
Associate Professor of Surgery
University of Toronto

“GI Cancer Genetics: Clinical Applications and Animal Models”

27 Anj Dlugosz, Ph.D.
Professor of Dermatology
University of Michigan

“Role of the Sonic Hedgehog Signaling Pathway in Skin: At the Crossroads of Development and Cancer”

**University of Michigan Comprehensive Cancer Center
Grand Rounds 1997-1998 (continued)**

MARCH

6	Harmon Eyre, M.D. Executive Vice President for Research and Cancer Control American Cancer Society	“Progression in the Control of Cancer”
13	Dean Brenner, MD Professor of Internal Medicine University of Michigan	“Cancer Chemoprevention: Problem and Opportunities”
20	Richard Wahl, M.D. Professor of Internal Medicine and Radiology University of Michigan	“Imaging Tumor Metabolism with PET”

APRIL

3	Owen Witte, M.D. Professor of Microbiology and Molecular Genetics, UCLA	“Signal Transduction Pathways in Lymphocyte Development and Response”
10	Jack Dixon, Ph.D. Professor of Biochemistry University of Michigan	“The Role of Reversible Phosphorylation in Cancer: Studies on the Ret Oncogene and Phosphatases Which Functions as a Tumor Suppressor Gene:”
24	Titia de Lang, Ph.D. Professor of Cell Biology and Genetics Rockefeller University	“Mechanisms of Telomere Function”

MAY

1	James Montie, M.D. Professor of Surgery University of Michigan	“Evolution of Management Strategies for Carcinoma of the Prostate”
8	Philip Kantoff, M.D. Director of Genitourinary Oncology Dana Farber	“Recent Development in Prostate Cancer”
29	Suyu Shu, Ph.D. Director of Research Cleveland Clinic Foundation	“Immunotherapy of Cancer with T Cells”

JUNE

5	Marc Lippman, M.D. Director of Georgetown University Lombardi Cancer Center	“Prospects for the Biologic Therapy of Breast Cancer”
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